Evaluation of Personalised Canine Electromechanical Models

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Abstract. Cardiac modelling aims at understanding cardiac diseases and predicting cardiac responses to therapies. By generating the electrical propagation, the contraction and the mechanical response, we are able to simulate cardiac motion from non-invasive imaging techniques. Four healthy canine clinical data (left ventricles) were provided by the STACOM'2014 challenge. Our study is based on Bestel-Clement-Sorine mechanical modelling, while the electrophysiological phenomena is driven by an Eikonal model. Our model has been calibrated by a quantitative sensitivity study as well as a personalized automatic calibration. Results and comparison with clinical measures are shown in terms of left ventricular volume, flow, pressure and ejection fraction.

1 Introduction

Cardiac modelling aims at understanding cardiac diseases (such as heart failure, desynchronization or tachycardia) and predicting cardiac responses to treatment or therapies (as cardiac resynchronization therapy or radiofrequency ablation). The goal is to help cardiologists in detecting anomalies, planning interventions, and selecting suitable patients for a given therapy. Cardiac modelling is driven by the assumption that the electromechanical response of the heart can be simulated from anatomical and physiological data.

Heartbeat is initiated by an electrical wave that propagates through the myocardium, activating mechanical contraction at a microscopic scale. A suitable model needs to take into account the anatomical structure, the electrical propagation, as well as the mechanical function of the heart.

Our study is based on an Eikonal model [3] for the simulation of the electrophysiological system, while the active and passive mechanical behavior is defined by the Bestel-Clement-Sorine modelling as formulated in [1]. The latter ensures to take into account the microscopic scale phenomena of the contraction as well as laws of thermodynamics.

The coupled electro-mechanical simulation of the cardiac system is implemented within the SOFA platform[1]. The simulations were performed on healthy

[1] SOFA is an Open Source medical simulation software available at http://www.sofa-framework.org

canine clinical data, provided by the STACOM'2014 challenge. They include Left Ventricular (LV) geometry, LV volume and LV pressure curves, as well as myocardial fibre directions.

2 Models and Methods

Canine and human hearts have close anatomical structures, that is why the canine heart is often used in pre-clinical studies. Both anatomies are composed of two ventricles, left (LV) and right (RV), and two atria. The heart function is mainly driven by the LV, acting like a pump to send the blood to the body. The system studied here is composed of a healthy canine left ventricle. In order to run the electrical and the mechanical cardiac models, input such as anatomical meshes and fibre directions have been processed.

2.1 Geometry Processing

Myocardial Mesh Generation. The myocardium mesh is generated using CGAL[2] meshing software, to create a tetrahedral mesh from medical image segmentations. The geometry is computed at end diastole (ED). The number of elements is roughly 50K, so that the average edge length is close to 1.5mm. This refinement ensures to have enough elements in the thickness of the muscle to describe the anisotropy (at least 5 layers transmurally) while limiting computation time.

In addition to the volumetric mesh segmentation, endocardial (inner lining) and epicardial (outer layer) surface zones are manually delineated, as illustrated in Fig. 1(a). These surface zones are useful for the electrical as well as for the mechanical simulations (Sec. 2.2).

For a single left ventricular model we consider that the contraction of the left ventricle does not depend on that of the RV as a first approximation. We depart from classic anatomical terminology in identifying the epicardium with the outer layer of the left ventricle segmentation.

Pericardium Surface Generation. Our model incorporates boundary conditions that faithfully replicate anatomical constraints on the motion of the heart. Specifically, the pericardial membrane is modelled as a fixed surface around the epicardium as in [2], and was obtained by dilating the segmentation from the diastasis phase of 1.5 mm, see Fig. 1(b)). The SOFA simulation platform allows for realistic collision constraints between the myocardium and the surrounding pericardium, which limits radial motion but also global translations. We model the presence of the RV as part of a pericardium membrane surrounding the LV. This is motivated by the fact that the pressure applied by the RV on the external wall of the LV could be approximated by a rigid constraint.

[2] CGAL is a Computational Geometry Algorithms Library, available at www.cgal.org.

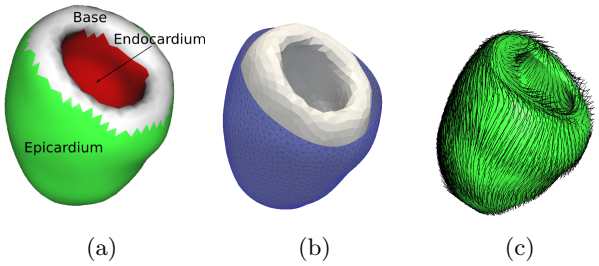


Fig. 1. Geometry and fibres processing: Identification of the surface zones of the LV myocardium mesh (a), pericardium surface membrane (b) and fibre directions from DTI imaging (c).

Fibre Directions. The myocardium is organized in muscle fibres which govern the electric propagation as well as the anisotropic contraction. The anisotropic tensor at each position can be measured via DTI imaging, and the principal directions (from eigen value decomposition) generate an approximation of the fibre directions. They are displayed in Fig. 1(c).

2.2 Electro-Mechanical Modelling: SOFA Software

The pipeline efficiently couples the simulation of the electrophysiology and mechanics of the heart in the SOFA platform. The electrical wave propagation is simulated in the ED configuration, during the first step of the cardiac cycle. The mechanical contraction and relaxation of the myocardium are simultaneously computed from the depolarization times output by the electrical simulation, taking into account the different forces and boundary conditions. The pipeline is summarized in Fig. 2.

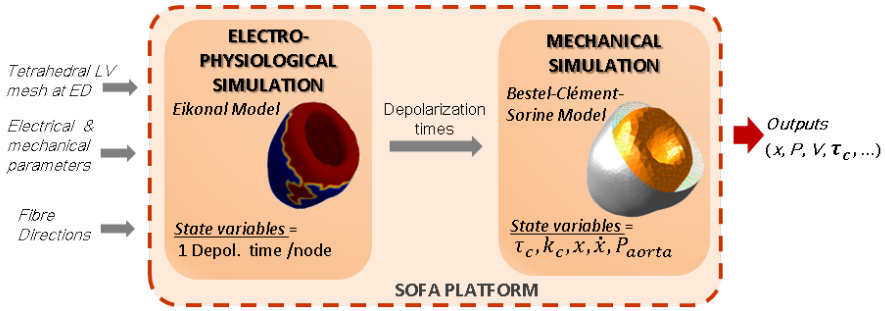


Fig. 2. Complete electromechanical pipeline. A single simulation computes simultaneously the electrical and the mechanical modellings.

Electrophysiological Simulation: Eikonal Model. The electrophysiological pattern of activity is simulated using an Eikonal model, describing the depolarization front propagation. The depolarization times T_d at each node of the mesh are estimated by solving the Eikonal equation $v\sqrt{\nabla T_d^t \mathbf{D} \nabla T_d} = 1$ using a Multi-Front Fast Marching Method [3]. v is the local conduction velocity, set here uniformly to 500 mm/s. D is the anisotropic tensor, with an anisotropic ratio of 0.1 between the fibre direction and the perpendicular directions, and with local fibre directions estimated according to section 2.1.

The initialization of the electric wave is set on the LV endocardial surface (see Fig. 1(a)), to simulate a simultaneous activation pattern of the endocardium from the extremities of the Purkinje network.

Mechanical Simulation: Bestel-Clement-Sorine Model. Our study is based on Bestel-Clement-Sorine (BCS) mechanical modelling as formulated by [1], improved and implemented on the SOFA platform by [2]. The BCS model is compatible with the laws of thermodynamics and it is based on the microscopic scale phenomena.

It is composed of a passive hyperelastic part described as a Mooney Rivlin material, that accounts for the elasticity. The stress along the cardiac fibres is decomposed into two parts. An active part models the contraction (binding/unbinding of actin-myosin filaments) together with an energy dissipation due to friction, and a parallel passive part corresponds to the elastic bound. The model is further improved by taking into account the circulation model representing the 4 phases of the cardiac cycle. Especially, the aortic pressure is modelled following a 2-parameter Winkessel model.

The BCS model is in particular able to capture the Starling effect (adaptation of the contraction enabling the stroke volume to compensate the end-diastolic volume) and the unbinding due to a too high relative speed between actin and myosin, with a constant α related to the cross-bridge release. For more details on the mechanical model, refer to [2].

3 Parameter Estimation

We use the approach described in [2] to estimate the parameters on canine hearts. Note that [2] was used to estimate parameters on human data and therefore cannot be applied as it is since the geometry, the cardiac period and the mechanical materials are different. A complete sensitivity study and a personalized calibration of the most relevant parameters have been performed.

3.1 Sensitivity Study

The parameters of the model are summarized in Tab. 1. The electrophysiological model is governed by a simple law, and has therefore mainly three parameters (once fibre directions and initial conditions are set), the local conduction velocity v, the anisotropic ratio A and the action potential duration (APDs). For

the mechanical part, the parameters can be separated in 3 groups: parameters related to the active contraction, parameters related to the passive material, and parameters related to the heamodynamic model.

Starting from the results of [2], a quantitative study has been performed in order to estimate the range of possible values of each parameter of Tab. 1. We used pressure and volume observations to control the simulation. Some parameters do not impact significantly the simulation, as the maximum stiffness k_0. Others are easily calibrated, because they are visually perceptible, as the APD.

	Parameter Name	**Unit**	case 1	case 2	case 3	case 4
Electric Part	A (Anisotropic Ratio)		0.1	0.1	0.1	0.1
	v (Local Conduction Velocity)	$mm.s^{-1}$	500	500	500	500
	APD (Action Pot. Duration)	s	0.18	0.18	0.20	0.24
Contraction	σ_0 (Max Contraction)	MPa	30	29	20	21
	k_0 (Max Stiffness)	MPa	6	6	6	6
	k_{ATP} (Contraction Rate)	s^{-1}	40	40	40	40
	k_{RS} (Relaxation Rate)	s^{-1}	90	90	90	90
	E (Linear Modulus)	MPa	5	5	5	5
	α (Cross-bridges Unfasten Rate)		0.8	0.8	0.8	0.8
	μ (Viscosity)	$MPa.s$	0.32	0.32	0.5	0.49
	n_0 (Reduc. factor, Starling effect)		0.5	0.5	0.5	0.5
Passive Mat.	$c1$, $c2$ (Mooney-R. Modulus)	kPa	50	50	50	50
	K (Bulk Modulus)	MPa	1.7	1.7	2	1.9
Windkessel	Rp (Wind. Resistance)	$MPa.m^{-3}.s$	179	250	310	430
	τ (Wind. Charact. Time)	s	0.22	0.16	0.23	0.56

Table 1. Parameters of the electro-mechanical model for the 4 cases.

3.2 Mechanical Parameters Calibration: Unscented Transform Algorithm

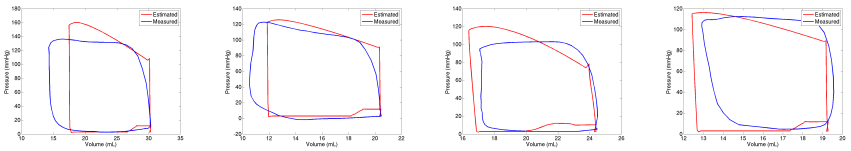
The most influential and independent parameters identified as [σ, μ, K] have been calibrated for each heart using the Unscented Transform Algorithm [4]. The algorithm, derived from the Unscented Transform according to [2], calculates a set of n parameters of a nonlinear transformation that minimizes the difference between the measured observations and the predicted observations. Once having performed $2n+1$ simulations using some specific parameter values, the algorithm runs in one iteration. In our case, the observations are the minimal LV outgoing blood flow and the ejection fraction. LV outgoing flow is calculated as $-dV/dt$, with V the LV volume.

Independently, the Unscented Transform algorithm was used to calibrate the 2-parameter Windkessel model using the ground truth pressure curves.

4 Results

4.1 Clinical Data

The STACOM 2014 challenge revolves on data acquired on 4 healthy canine hearts. They include LV geometry and fibre directions. The 4 dogs were paced at 500ms basic cycle length. The tetrahedral mesh is constructed from binary images of the LV at ED.



(a) case 1 (b) case 2 (c) case 3 (d) case 4

Fig. 3. Comparison between LV pressure volume diagrams computed from simulations (red) and ground truth measures (blue).

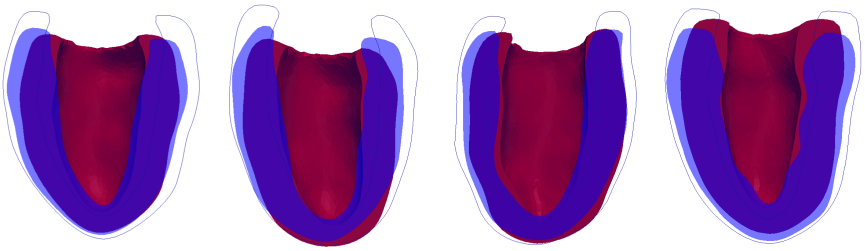
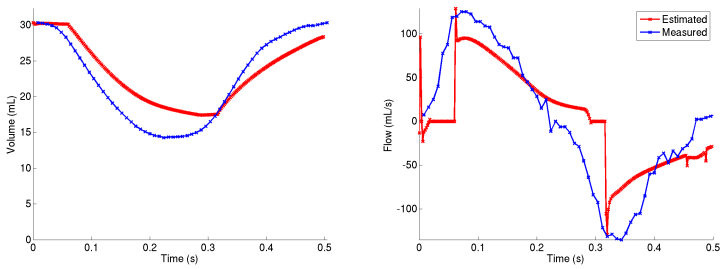


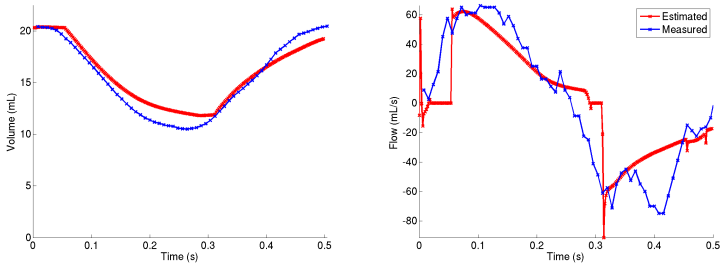
Fig. 4. Simulated end-systolic geometry (red) of the LV of the 4 cases and ground truth (blue). The dark blue line represents the initial position (ED).

4.2 Current Results

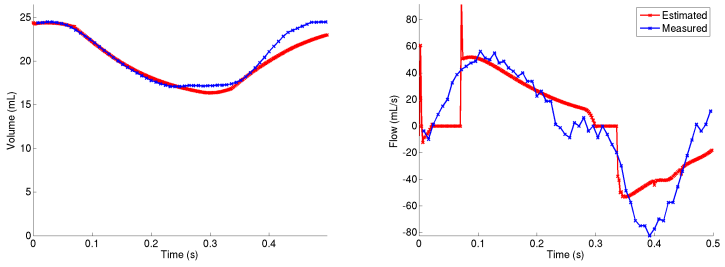
We give the results of the 4 canine simulations in terms of LV pressure volume diagrams (Fig. 3), LV volume, LV outgoing flow curves (Fig. 5) and ejection fractions (Tab.2). Comparison is made with the ground truth data, as LV volume and LV pressure curves were provided by the STACOM'2014 challenge for a complete cycle. We are displaying here the second cycle of the simulation, in order to avoid the wrong initial conditions.



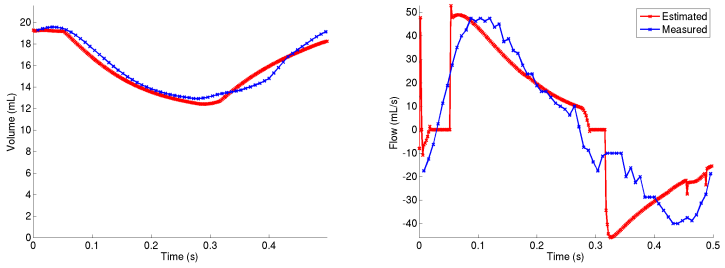
(a) case 1



(b) case 2



(c) case 3



(d) case 4

Fig. 5. Comparison between LV volume and outgoing flow (as $-dV/dt$) variations over one cardiac cycle computed from simulations (red) and ground truth measures (blue).

The simulated geometry of the 4 cases at ES is shown in Fig. 4. The ground truth end-systolic position is shown in blue while red is the simulation. The dark blue line represents the initial position (ED).

4.3 Discussion and Improvements

This first study shows promising results: the LV pressure volume diagrams and volume variations comparison indicate a realistic response of the model. Furthermore, the large variability of ejection fraction is reproduced in our results. We can also see from the slices of Fig. 4 that the modelled ventricle has a realistic movement (note the correct apico-basal shortening). However, the myocardium wall thickness variation is not completely reproduced, corresponding to a simulated muscle not incompressible enough.

Ejection fraction	case 1	case 2	case 3	case 4
Measured (%)	53	49	30	34
Estimated (%)	43	42	33	36

Table 2. Comparison between ejection fractions computed from the simulations and the ground truth measures.

The calibration of a model of a standard case is the first step towards the prediction of its response to treatments and therapies. Since our model is driven by faithful anatomical constraints and mechanical laws, we are confident in the fact that such a model will be able to realistically simulate pathology cases and predict their responses to treatments.

5 Conclusions

In this paper we have adapted an electro-mechanical cardiac modelling to canine hearts. From the geometry of the left ventricle in end diastole and the heart period and the fibre directions, we are able to simulate heart movement over the whole cardiac cycle. The quantitative validation (results of the STACOM'2014 challenge) is comforting the tendency of the global indicators: the displacement fields obtained with the simulations and the displacement fields obtained by tagged MRI provided by the STACOM'2014 challenge are in good agreement.

Acknowledgments

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